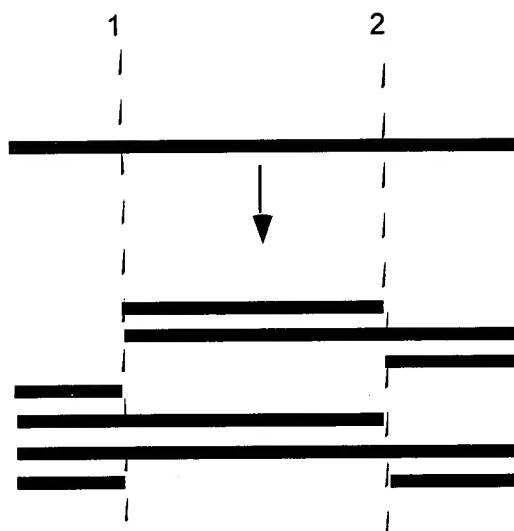


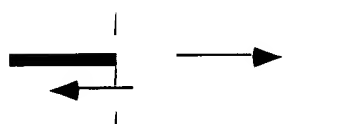
(A)

All possible recombinants
prepared by crossover
at positions 1 and 2



(B)

These can be prepared by
assembly of synthetic
fragments containing the
crossover positions



Requires fragments
(plus end primers):



FIG. 7

Extension of synthetic
fragments against a
parent template strand
and gap repair

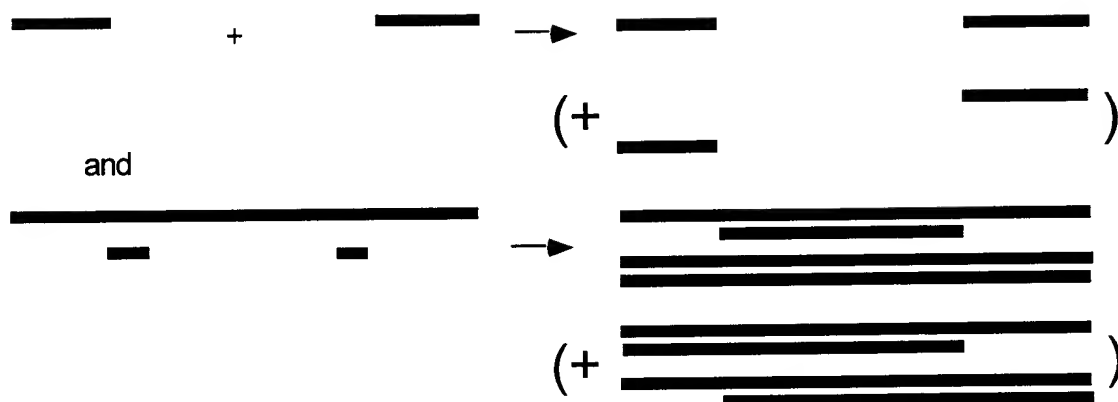
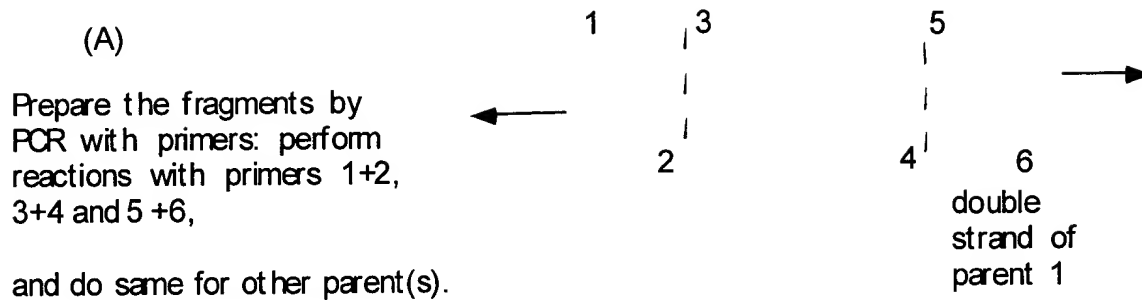


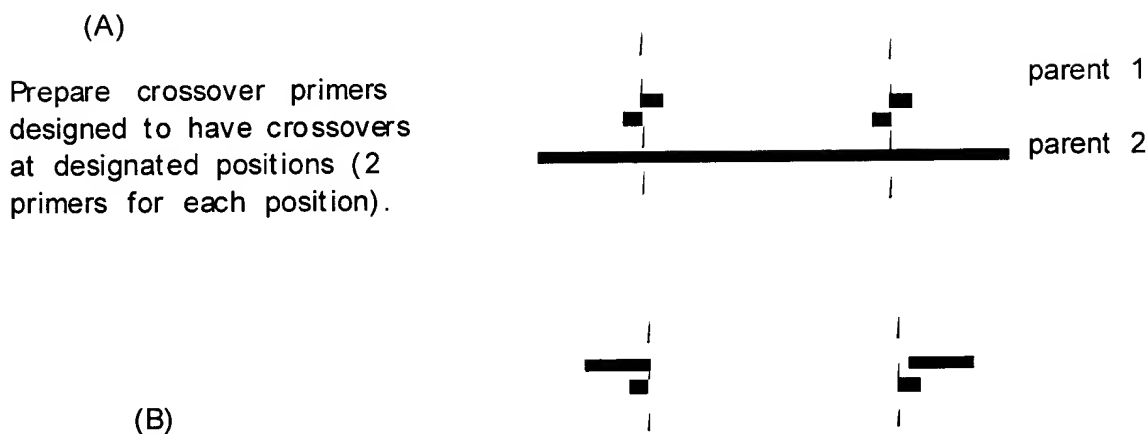
FIG. 8



(B)

Reassemble fragments in a pool, by PCR with 1+ 6

FIG. 9

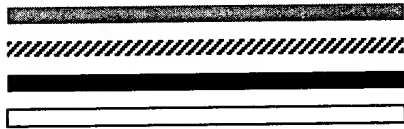


Fragment parent genes and PCR reassemble in the presence of the crossover primers to promote recombination at designated positions

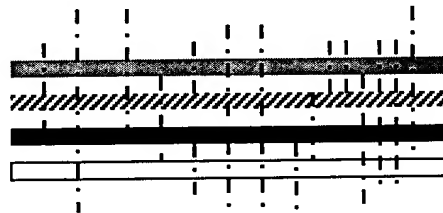
FIG. 10

Recombinant search algorithm

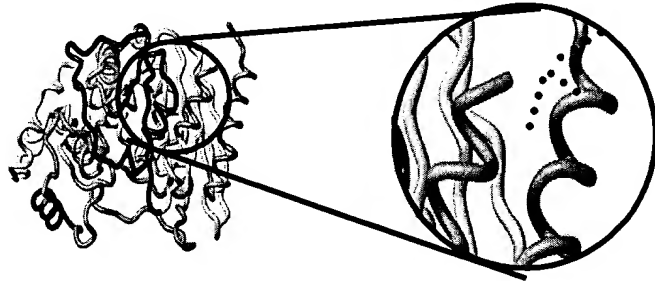
1. Align parent sequences with template structure



2. Determine all possible crossover points according to sequence identity algorithm



3. Calculate coupling matrix



4. Pick start parent at random and copy to offspring until a possible cut point is reached

5. Pick random number, if less than p , copy random new parent until next cut point is reached.

6. Determine crossover disruption of offspring gene

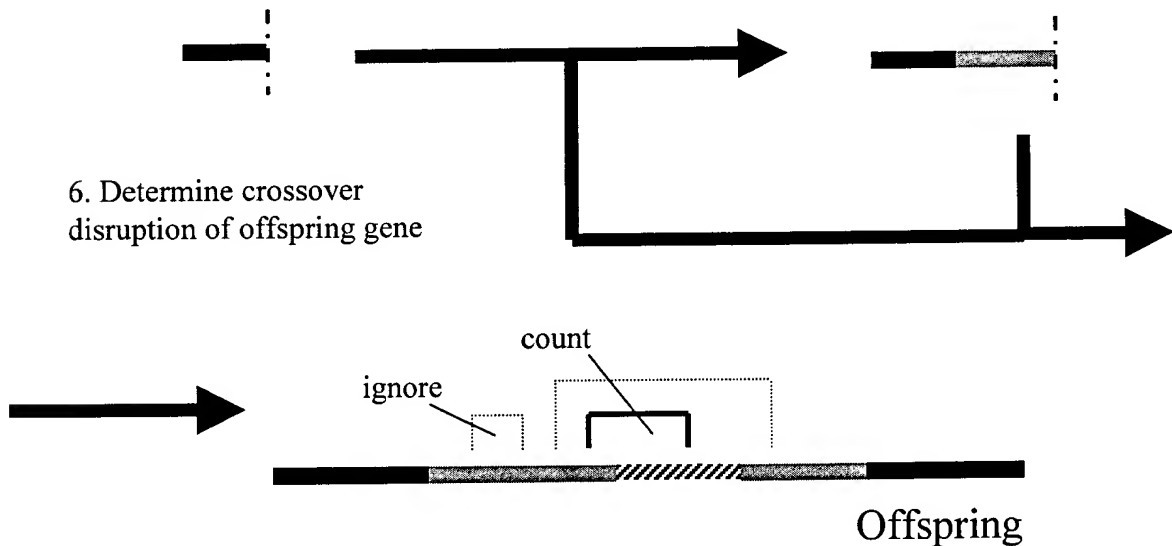


FIG. 12

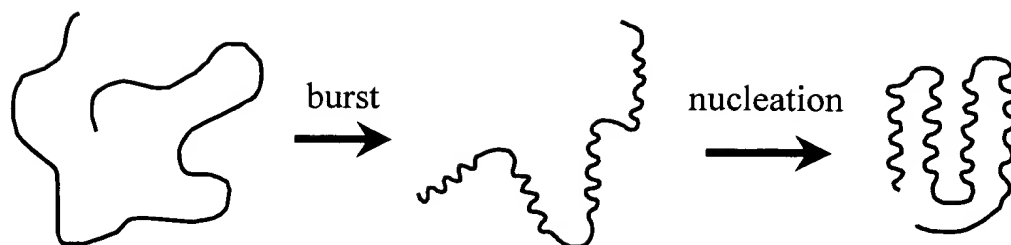


FIG. 18

The contact map shows residues that are distant (black) and residues that are close (white). If a given segment, , folds an above average number of residues into a given sphere size, then it is compact.

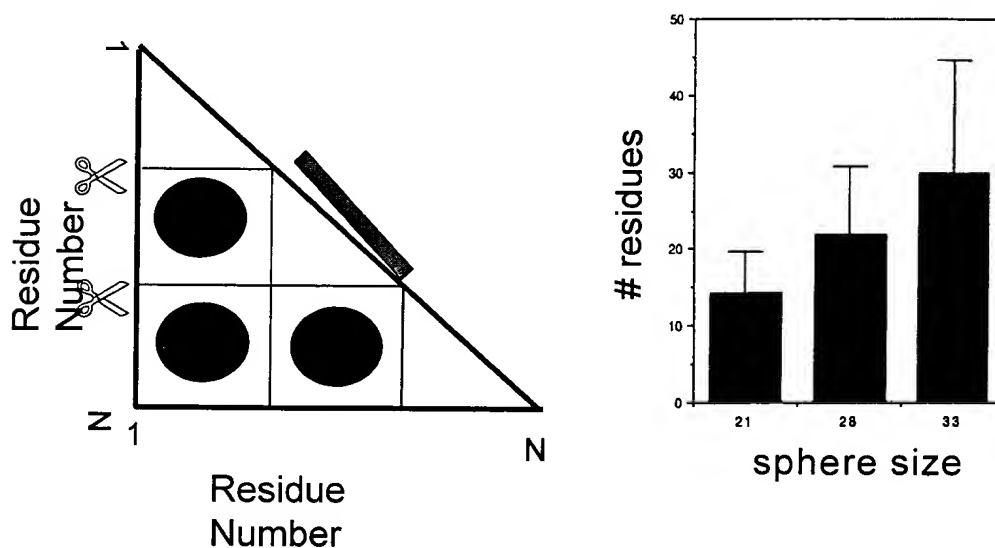


FIG. 19

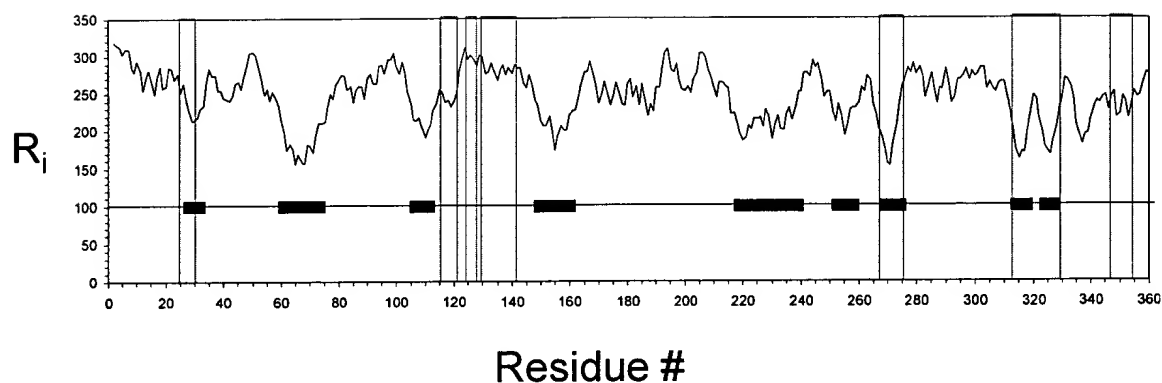
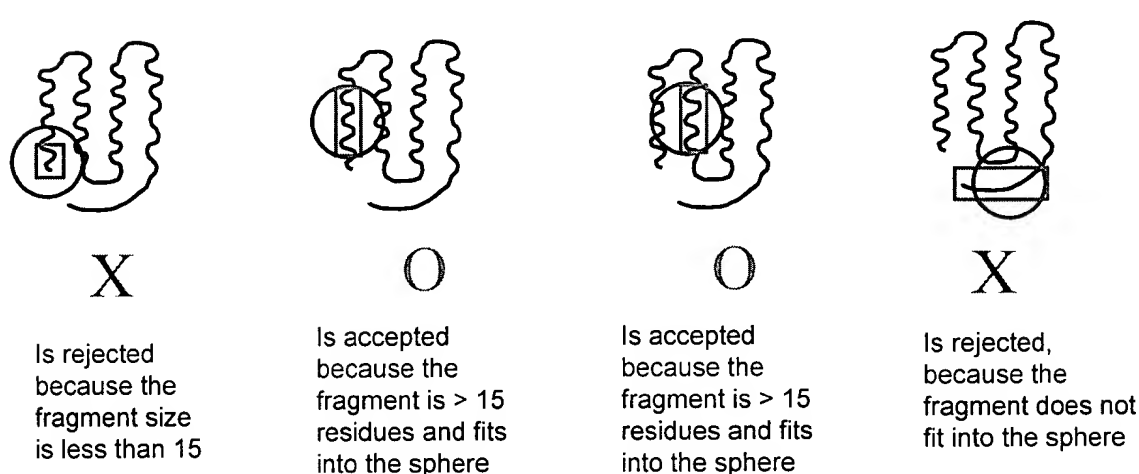


FIG. 22



(1) Pick a sphere size (21 angstroms, like Go-Gilbert) and a disruption threshold; (2) Scan protein using segments at least the average number of residues for that sphere size or greater (e.g., >15 for 21 angstrom sphere); (3) Check the disruption of all the compact fragments identified in step 2. If the fragment has a disruption above a threshold value, keep it; otherwise, throw it out; (4) If the compact unit is disruptive, increment the schema disruption measure for all of the residues in the fragment by one. This indicates that crossovers within the fragment are disfavored.

FIG. 23